

NINDS Notes



National Institute of Neurological Disorders and Stroke

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Note to Subscribers:

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ALSA Funds Partnership Effort to Find Genes Involved in Sporadic ALS

In a cooperative effort that promises new targets for effective therapeutics for amyotrophic lateral sclerosis (ALS), the ALS Association (ALSA) recently announced funding of a search for genes involved in the sporadic form of the disorder in people who have no family history of the disease. The study uses the most up-to-date technology of gene finder chips

The search will use the newly established DNA banking project—a repository of samples from patients and healthy people for comparison—made possible through the National Institute of Neurological Disorders and Stroke (NINDS). At the National ALS Advocacy Day and Public Policy Conference held on May 15-17, 2006, in Washington D.C., ALS patients and caregivers participated by anonymously donating a small amount of blood and providing a clinical history. In order to protect privacy, none of the gathered information allows the donors to be individually identified.

Investigators Bryan Traynor, M.D., a fellow at the National Institute of Mental Health, and John Hardy, Ph.D., of the National Institute on Aging (NIA), will lead the joint effort with NINDS and the Robert Packard ALS Center at Johns Hopkins University. The work will be carried out at the NIA Neurogenetics Laboratory, Bethesda, Md.

“We are extremely pleased to have such an excellent team for a partnership that is truly using cutting edge technology,” said Lucie Bruijn, Ph.D., ALSA science director and vice president. “This effort should make a real difference for sporadic ALS and is the kind of project that the patient DNA repository was put in place to serve.”

Bruijn noted that the information gathered by the partnership will be made readily available to other scientists in the field.

ALS is inevitably fatal and despite numerous research advances no treatments have been found. It remains a mystery why nerve cells that supply muscles die in the disease. Scientists are still challenged to come up with an effective, targeted therapy.

In the decade since the discovery of a mutation in the protein copper-zinc superoxide dismutase (SOD1), the cause of some inherited forms of ALS, several more mutations have been brought to light. Finding genes that contribute to the disorder undoubtedly will provide new targets for therapeutic candidates.

The genetic underpinnings of sporadic ALS—the disease that for 90 percent of ALS patients appears to occur spontaneously without family history—remain even more unclear. Even though inherited ALS is clinically indistinguishable from sporadic ALS, the same genes may not be responsible for both. But something that is common to both forms of the disease is the way that motor neurons die. That is why a gene change identified in one type can help understand the other.

Is sporadic ALS due to a gene change, several gene changes that interact, an environmental exposure, or some combination of these factors? Traynor and Hardy will take on the challenge of sporadic ALS directly by using the newest technology to search through the entire genome of more than 500 people who will contribute

samples. Thanks to the Human Genome Project and a new technology that accelerates the ability to sift through the genome, the ability to seek signposts of gene change among samples from many people at once should help address the mystery behind sporadic ALS.

The team will search through variations in the genes called single nucleotide polymorphisms (SNPs). These SNPs each represent an instance where the genetic code for an individual has a difference at one particular base in the DNA. The Human Genome Project identified large numbers of SNPs distributed among the genes in humans. SNPs can serve as signposts on chromosomes of places that could end up including a gene linked with ALS. SNPs tell scientists where in the vast genome to start looking.

The investigators will carry out automated analysis of samples collected by the ALS Biomaterial and Data Banking initiative, part of the NINDS Human Genetics Repository, using the newest SNPs on a chip. A SNP chip is a device similar to a computer chip that can read known SNPs in the human genome. The technology to be used in the effort offers unprecedented detailed analysis of the SNPs present in the human genome. Operated by robotics, a search through 276 U.S. ALS patient samples and 276 European patient samples should produce important new information on what genetic influences might be producing sporadic ALS.

Because the NINDS repository includes data on the symptom onset, progression, laboratory findings, and other features of the illness, and in normal subjects, detailed medical and family history, the DNA samples will be analyzed with correlations to clinical symptoms adding to the strength of this study.

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Applications Sought for Collaborative Awards in Epilepsy Research for Junior Investigators

The National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute on Aging (NIA) invite applications for collaborative awards in epilepsy research for junior investigators.*

Epilepsy, characterized by repeated uncontrolled seizures, is one of the most common neurological disorders in the United States. It currently afflicts approximately 15 million Americans of all ages and backgrounds. Despite many decades of research, new anticonvulsant drugs, and advances in surgical therapy, a large number of people with epilepsy suffer from uncontrolled seizures or the side effects of drugs or surgical treatment.

Potential research areas include, but are not limited to: mechanisms for interrupting or modifying the process of epileptogenesis; identification and characterization of genetic mutations that are the basis of inherited forms of epilepsy and that can provide a means of understanding the causes of seizures and determining treatment strategies; studies of the basic biology of neural development and aging that might contribute to identification of the molecular basis for abnormalities observed in some people with epilepsy; visualization of structural and functional changes in the brains of people with epilepsy using advanced imaging technologies such as magnetic resonance spectroscopy, functional magnetic resonance imaging, and magnetoencephalography; development of new classes of pharmacological agents and other effective therapeutic strategies such as focal brain stimulation and brain irradiation; and innovative clinical trial methodologies to quickly identify effective antiepileptogenic interventions.

For more information, potential applicants should contact Margaret Jacobs, Program Director, Channels, Synapses, and Circuits Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2138, Bethesda, MD 20892; telephone: 301-496-1917; fax: 301-402-1501; e-mail: mj22o@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PA-06-190.html>.

Applications Sought for the Exploratory/Developmental Program for Translational Research in Muscular Dystrophy

The National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), and the National Institute of Child Health and Human Development (NICHD) encourage applications for the exploratory/developmental program for translational research in muscular dystrophy.*

The muscular dystrophies are progressive, degenerative disorders affecting skeletal and cardiac muscle. Despite substantial research efforts, there are few therapies that are effective in even slowing the course of the disorders. The purpose of this announcement is to exploit the accumulated knowledge of the genetic basis and pathogenic mechanisms in the muscular dystrophies to design and test treatments with potential for reducing the clinical burden of disease.

Areas of research interest include, but are not limited to: development of drug-based therapies to protect muscle mass; development of strategies to enhance existing muscle repair mechanisms; optimizing cell-based muscle replacement strategies; developing, testing, and improving strategies for gene replacement therapy; developing and testing genetic modification therapies to bypass inherited mutations; and developing combination therapies that rely on more than one of the strategies listed above in order to produce a more effective treatment than may be possible with any single strategy.

For more information, potential applicants should contact Dr. John Porter, Program Director, Channels, Synapses, and Circuits Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2142, Bethesda, MD 20892; telephone: 301-496-1917; fax: 301-402-1501; e-mail: jp477n@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAR-06-203.html>.

Research Sought on Ethical Issues in Human Subjects Research

The National Institute of Neurological Disorders and Stroke (NINDS) encourages applications for research on ethical issues in human subjects research. This announcement is made together with 16 other components of the National Institutes of Health (NIH) and is supported by 3 grant funding mechanisms: R03, R21, and R01.*

Recent developments in biomedical and behavioral research—which include the rapid growth of new interventions and technologies, increasing involvement of foreign populations in human subjects research, and concerns about financial conflicts of interest among researchers—challenge the ability of investigators to interpret and apply the regulations. Other situations may present difficulties for identifying strategies, procedures, and/or techniques that will enhance or ensure the ethical involvement of human subjects in research. Thus, research on ethical issues in human subjects research is necessary to enhance interpretation and application of ethical principles and regulatory requirements.

Topics of research interest include, but are not limited to: assessing risks in human subjects research; issues in informed consent; international research; study design in clinical trials and its relationship to medical care; research oversight: IRBs, DSMBs, and COI committees; research with specimens and data; and dissemination of research findings.

For more information, potential applicants should contact Dr. Barbara Radziszewska, Clinical Research Project Manager, Clinical Trials Group, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2216, Bethesda, MD 20892; telephone: 301-496-2076; fax: 301-480-1080; e-mail: br94h@nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at:

<http://grants.nih.gov/grants/guide/pa-files/PA-06-367.html> (R03),

<http://grants.nih.gov/grants/guide/pa-files/PA-06-368.html> (R21), or

<http://grants.nih.gov/grants/guide/pa-files/PA-06-369.html> (R01).

NIH Clinical Trial Planning Grant Program Applications Sought

The National Institute of Neurological Disorders and Stroke (NINDS) encourages applications for clinical trial planning grants. This announcement is made together with 9 other components of the National Institutes of Health (NIH).*

An NIH-defined phase III clinical trial is a broadly based prospective clinical investigation—usually involving several hundred or more human subjects—that evaluates an experimental intervention by comparing it with a standard or control intervention, or that compares two or more existing treatments. Often, the aim of such investigation is to provide evidence leading to a scientific basis to consider a change in health policy or standard of care.

The purpose of NIH clinical trial planning grants is to provide support for the development of a phase III clinical trial, including establishment of the research team, development of tools for data management and oversight of the research, definition of recruitment strategies, and finalization of the protocol and other essential elements of the study included in a manual of operations/procedures (MOP).

Activities supported by this funding initiative include, but are not limited to: developing and finalizing the MOP; finalizing plans for addressing federal and NIH gender and minority inclusion and human subjects protection requirements; establishing collaborative arrangements; instituting means to assure standardization of procedures across sites and among staff; developing tools needed for data collection and management; developing and finalizing safety and monitoring plans; and developing plans for training that may be required to carry out the proposed trial.

For more information, potential applicants should contact Dr. Scott Janis, Clinical Research Project Manager, Clinical Trials Group, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2191, Bethesda, MD 20892; telephone: 301-496-9135; fax: 301-480-1080; e-mail: sj151t@nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PA-06-363.html>.

Research Sought on Axonal Damage in Multiple Sclerosis

The National Institute of Neurological Disorders and Stroke (NINDS) invites grant applications for research on axonal damage in multiple sclerosis (MS) and strategies for protection and repair.*

MS is the second most common neurological disorder leading to disability in young adults, surpassed only by trauma. The disease is characterized by chronic inflammation and demyelination of the central nervous system (CNS) that over time may result in neurodegeneration. While axonal damage and neuronal cell death are likely to be the major cause of disability in the later, progressive phase of MS, new evidence suggests that even at early stages severance of nerve axons may occur and lead to irreparable nerve damage. Currently available therapies do not appear to significantly impact this tissue loss.

Areas of interest include, but are not limited to: therapeutic strategies for interference with molecular signals blocking axonal repair such as CNS myelin-associated inhibitors and glial scar-associated inhibitors; strategies promoting axonal maintenance and repair in demyelinating disease via delivery of trophic factors or the manipulation of a dysregulated signaling environment; translational or clinical research on the effects of channel blockers on axonal regeneration; development of delivery systems to target neuroprotective and regenerative compounds to MS lesions; exogenous strategies for the delivery of myelin forming cells such as transplantation of stem cells, oligodendrocyte progenitors, olfactory ensheathing cells, neurospheres, and Schwann cells; development of experimental models that mimic the axonal pathology of MS and allow the targeted study of approaches towards neuroprotection, repair, and remyelination under chronic inflammatory conditions; and development and improvement of imaging techniques that allow the characterization and quantification of MS tissue damage and the evaluation of repair strategies.

For more information, potential applicants should contact Dr. Ursula Utz, Program Director, Neural Environment Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2134, Bethesda, MD 20892; telephone: 301-496-1431; fax: 301-480-2424; e-mail: uulp@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAS-06-266.html>.

Research Sought on Neurovascular Mechanisms of Brain Function and Disease

The National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute on Aging (NIA) encourage grant applications for research on the neurovascular mechanisms of brain function and disease.*

Stroke is widely recognized as a major cause of premature mortality and disability, particularly cognitive and motor impairment. Significant progress has been made in dissecting the molecular pathways of excitotoxicity, oxidative stress, and apoptosis in ischemic neuronal cell death. However, translation of these laboratory results into clinically effective stroke treatments remains a major challenge for the stroke community. The purpose of this announcement is to achieve a better understanding of the integration of cerebrovascular and brain mechanisms in developing the healthy brain, in maintaining function in the aging brain, and in neurological disorders and stroke.

Research areas of interest include, but are not limited to, studies to: develop and characterize in vivo and in vitro models that reflect the unique features of neurovascular communication in the brain under normal, aging, and disease conditions; examination of the genes and proteins that are uniquely expressed by the neurovascular unit (NVU) and mechanisms by which brain cells regulate endothelial cell gene expression and vice versa; explore the genesis and regulation of the NVU, its stem cell origins, and the interactions of microvessel networks in the regions of the central nervous system with developing neurons and in areas of adult neurogenesis; identify signal transduction pathways of brain and capillary endothelial cells in the regulation of the extracellular matrix under normal and disease conditions; identify regional diversity of NVU properties within the brain and the microvasculature throughout the lifespan; identify changes in NVU integrative functions in vivo and/or in situ using imaging approaches; explore the cell-cell interactions among the cellular and matrix elements of the NVU; and examine cell-cell communication in tri-cultures with matrices of different composition.

For more information, potential applicants should contact Dr. Thomas Jacobs, Program Director, Neural Environment Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2112, Bethesda, MD 20892; telephone: 301-496-1431; fax: 301-480-2424; e-mail: tj12g@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAS-06-200.html>.

Research Sought on Understanding and Preventing Brain Tumor Dispersal

The National Institute of Neurological Disorders and Stroke (NINDS) and the National Cancer Institute (NCI) encourage applications for research on understanding and preventing brain tumor dispersal.*

Many brain tumors are highly invasive and therefore extremely difficult to treat. Cells from the primary tumor often infiltrate surrounding brain tissues, so that removal of the main tumor mass is not sufficient to prevent recurrence. The goal of this announcement is to promote studies that identify the properties of brain tumor cells that cause them to migrate, determine how interaction of tumor cells with normal brain elements affects migration, and translate understanding of these parameters into interventions that target invading tumor cells.

Possible areas of research interest include, but are not limited to: analysis of candidate genes and signal transduction pathways that control brain tumor cell dispersal; genomic or proteomic expression profiling aimed at identifying novel genes or proteins that control brain tumor cell dispersal; determination of the cells of origin and specific properties of migrating brain tumor cells; studies of extracellular matrix properties that potentially control normal and aberrant migration of cells in the CNS; determination of what causes brain tumor cells to exit the cell cycle during migration and reenter it during subsequent cell proliferation; studies of neural progenitor cell biology that may shed light on brain tumor dispersal; investigation of why invading brain tumor cells are resistant to chemotherapy or radiation; and development of novel methodologies that permit more effective visualization of migrating brain tumor cells.

For more information, potential applicants should contact Dr. Jane Fountain, Program Director, Neural Environment Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2110, Bethesda, MD 20892; telephone: 301-496-1431; fax: 301-480-2424; e-mail: jf227t@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAS-06-201.html>.

Research Sought on Non-Human Lentiviral Models of the Neurological Complications of AIDS

The National Institute of Neurological Disorders and Stroke (NINDS), the National Institute on Drug Abuse (NIDA), and the National Institute of Mental Health (NIMH) encourage grant applications for research on non-human lentiviral models of the neurological complications of AIDS. This announcement is supported by 2 grant funding mechanisms: R03 and R21.*

Neurological dysfunction is a devastating complication of HIV/AIDS, affecting more than 25 percent of chronically infected individuals. Symptoms include cognitive deficits, motor impairment, and peripheral neuropathies.

Areas of research interest include, but are not limited to: studies to define the pathogenic mechanisms of lentiviruses in the central nervous system (CNS) of animals temporally during the progression of disease; in vivo studies of host and viral factors affecting the penetration of lentiviruses and infected cells across the neuroprotective blood-brain barrier; use of non-human animal models to define and characterize novel markers associated with disease progression and response to therapeutic interventions; development of non-human animal models of peripheral neuropathy caused by lentiviral infection; use of lentiviral models for concurrent study of neurologic complications in animals repetitively exposed to substances of abuse, such as methamphetamine, opiates, cocaine, and marijuana, or withdrawn from such substances; and in vivo studies of glial-neuronal interactions in models of lentiviral infection and their complication by drugs of abuse.

For more information, potential applicants should contact Dr. Michael Nunn, Program Director, Neural Environment Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2115, Bethesda, MD 20892; telephone: 301-496-1431; fax: 301-402-2060; e-mail: mn52e@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAS-06-275.html> (R03), or <http://grants.nih.gov/grants/guide/pa-files/PAS-06-276.html> (R21).

Preclinical Therapeutics Development for NeuroAIDS Sought

The National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Mental Health (NIMH), and the National Institute of Drug Abuse (NIDA) invite applications for preclinical therapeutics development for neuroAIDS. This announcement is supported by 2 grant funding mechanisms: R03 and R21.*

Since the availability of the first antiretroviral therapy in 1987 and sequential discoveries of other antiretroviral agents, there has been a dramatic decrease in mortality and morbidity among the HIV/AIDS population. However, despite these important advances, the prevalence of HIV-associated mental and neurological disorders is increasing, in part, because of the prolonged lifespan of infected patients.

Research areas of interest include, but are not limited to: the development of in vitro assays or cell systems that detect HIV replication or activation in appropriate central nervous system (CNS) or CNS-related/derived cell types; studies to devise new approaches for increasing the permeability of antiretroviral agents or other related therapeutic compounds through the blood-brain barrier (BBB); studies to address the effects of drugs of abuse on the BBB; the development of animal models of HIV neuropathogenesis ultimately for use in screening therapeutic compounds or treatment strategies; validating existing animal models of HIV/SIV pathogenesis for use in screening the therapeutic potential of compounds or treatment strategies; the development of new models or validation of existing models of HIV neuropathogenesis in the context of drug abuse or withdrawal for use in screening the therapeutic potential of compounds or treatment strategies appropriate for the drug-addicted population; and the development of novel models of toxicity that are sensitive to CNS developmental stages and vulnerabilities.

For more information, potential applicants should contact Dr. Michael Nunn, Program Director, Neural Environment Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2115, Bethesda, MD 20892; telephone: 301-496-1431; fax: 301-402-2060; e-mail: mn52e@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PA-06-140.html> (R03), or <http://grants.nih.gov/grants/guide/pa-files/PA-06-139.html> (R21).

Research Sought on Mechanisms of Transmission and Dissemination of Transmissible Spongiform Encephalopathies

The National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute on Aging (NIA) invite applications for research on mechanisms of transmission and dissemination of transmissible spongiform encephalopathies (TSEs). This announcement is supported by 2 grant funding mechanisms: R03 and R21.*

TSEs or “prion diseases” are neurodegenerative disorders that can lead to dementia, motor dysfunction, and, eventually, death. The best known mechanism of natural transmission of TSEs is via the gastrointestinal tract through ingestion of contaminated food. Once in the digestive tract, prions are able to disseminate to the peripheral lymph organs and the central nervous system (CNS). The purpose of this announcement is to expand research on how these diseases can spread within an affected population and how infectious prions are then distributed through the body and ultimately to the CNS.

Research areas of interest include, but are not limited to: the natural spread of TSEs within species; the spread of TSEs across species barriers; the mechanisms involved in the transport of prions from the gastrointestinal tract, or other mode of entry, to the CNS; the roles of age-related factors in the transport and entry into the CNS and the consequent pathological manifestations; the possible involvement of inflammatory or other cofactors in the dissemination of TSE agents; and animal models aimed at understanding the mechanisms of transmission and dissemination of TSEs.

For more information, potential applicants should contact Dr. Michael Nunn, Program Director, Neural Environment Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2115, Bethesda, MD 20892; telephone: 301-496-1431; fax: 301-402-2060; e-mail: mn52e@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PA-06-192.html> (R03), or <http://grants.nih.gov/grants/guide/pa-files/PA-06-193.html> (R21).

Research Sought for Understanding and Treating Tuberous Sclerosis Complex

The National Institute of Neurological Disorders and Stroke (NINDS) invites grant applications for research on understanding and treating tuberous sclerosis complex (TSC). This announcement is made together with 4 other components of the National Institutes of Health (NIH) and is supported by 2 grant funding mechanisms: R03 and R21.*

The genes that cause TSC (TSC1 and TSC2) are known, understanding of the pathways in which they act is increasing, and animal models that mimic certain features of the disease now exist. As a result, there is a remarkable opportunity to increase knowledge about the mechanisms that cause TSC and translate that knowledge into therapies for this often devastating disorder.

Topics of research interest include, but are not limited to: studies of the role of hamartin and tuberin in basic cellular processes and development; development of more sophisticated animal models for TSC; development of cell culture models of TSC; identification of the downstream targets of tuberin and hamartin, with particular emphasis on potential molecular targets for drug therapy; elucidation of the molecular events that cause lesions to develop in specific tissues; and assessment and treatment of TSC-associated cognitive and behavioral problems, including both pharmacological and non-pharmacological interventions.

For more information, potential applicants should contact Dr. Jane Fountain, Program Director, Neural Environment Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2110, Bethesda, MD 20892; telephone: 301-496-1431; fax: 301-480-2424; e-mail: jf227t@nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at:

<http://grants.nih.gov/grants/guide/pa-files/PAS-06-205.html> (R03), or
<http://grants.nih.gov/grants/guide/pa-files/PAS-06-206.html> (R21).

Applications Sought for Alzheimer's Disease Drug Discovery

The National Institute of Neurological Disorders and Stroke (NINDS), the National Institute on Aging (NIA), and the National Institute of Mental Health (NIMH) invite grant applications for Alzheimer's disease (AD) drug discovery.*

AD is one of the most persistent and devastating disorders of old age because it eventually leads to a complete loss of memory and the ability to function independently. An estimated four and a half million people in the United States have AD in its various stages and a projected 14 million people and their families could be affected by AD by the middle of this century if no new treatments are developed. The purpose of this announcement is to stimulate the discovery, development, and preclinical testing in cellular, tissue, and animal models of novel compounds for the prevention and treatment of the cognitive impairment and behavioral symptoms associated with AD.

The development of compounds for ameliorating, modifying, or improving potential aberrations in neuronal cellular communication mechanisms is encouraged. These compounds should be designed to affect fundamental processes, such as the neuronal dysfunction, death, and loss of connectivity associated with the disease by targeting molecules and mechanisms such as neurotransmitters, neuromodulators, and neurotrophins; receptors and ion channels; second and third messenger systems; all facets of relevant amyloid precursor protein, amyloid beta protein, and tau neurobiology; protein synthesis, aggregation, and degradation; energy utilization; and oxidative, immunological, and inflammatory mechanisms.

For more information, potential applicants should contact Dr. Diane Murphy, Program Director, Neurodegeneration Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2222, Bethesda, MD 20892; telephone: 301-496-5680; fax: 301-480-1080; e-mail: dm152o@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAS-06-261.html>.

Research Sought on the Cognitive Sequelae of Parkinson's Disease

The National Institute of Neurological Disorders and Stroke (NINDS), the National Institute on Aging (NIA), and the National Institute of Nursing Research (NINR) invite grant applications for research on the cognitive sequelae of Parkinson's disease (PD). This announcement is supported by 2 funding mechanisms: R03 and R21.*

PD is commonly viewed as a motor disorder, however, it also affects thinking, reasoning, learning, processing speed, and other cognitive abilities. The cognitive changes seen in people with PD are less understood and studied than the motor symptoms.

Areas of research interest include, but are not limited to: basic molecular or cellular studies of potential drugs or other treatments that could address cognitive impairments in PD; behavioral and physiological characterization of models based on the new molecular understanding of synuclein, parkin, and other proteins involved in the pathogenic processes of neurodegenerative disorders; development of relevant animal models for studying cognitive deficits in PD; preclinical studies of cognitive tests and paradigms in animal models of PD; studies of neuroprotective or other agents in animal models of PD with induced cognitive deficits; investigations of the relationship between age of onset of PD and PD-related cognitive changes; studies of neuroanatomical circuits and neurochemical processes mediating cognitive states and cognition-based individual differences in PD; examination of the specific consequences of deep brain stimulation or other surgical interventions on the cognitive aspects of PD; and development of assessment tools for detection of early cognitive change in people with PD.

For more information, potential applicants should contact Dr. Debra Babcock, Program Director, Systems and Cognitive Neuroscience Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2108, Bethesda, MD 20892; telephone: 301-496-9964; fax: 301-402-2060; e-mail: db390r@nih.gov; or Dr. Diane Murphy, Program Director, Neurodegeneration Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2222, Bethesda, MD 20892; telephone: 301-496-5680; fax: 301-480-1080; e-mail: dm152o@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PA-06-194.html> (R03), or <http://grants.nih.gov/grants/guide/pa-files/PA-06-195.html> (R21).

Research Sought on Rett Syndrome and MECP2

The National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Mental Health (NIMH), and the National Institute of Child Health and Human Development (NICHD) encourage grant applications for basic and clinical research on Rett syndrome (RTT) and MECP2. This announcement is supported by 2 grant funding mechanisms: R03 and R21.*

RTT is a severely debilitating neurodevelopmental disorder. Girls with RTT appear to develop normally until about 6 to 18 months of age at which time they enter a period of regression, losing speech, purposeful hand and motor skills, and cognitive abilities that they had acquired, while also developing seizures, repetitive hand movements, and other motor disturbances, autonomic dysfunctions such as breathing irregularities, social withdrawal (including autism), and growth and mental retardation. There is no cure for RTT; current treatment is symptomatic.

Possible areas of research interest include, but are not limited to: developmental, neuroanatomical, osteological, electrophysiological, and imaging studies intended to identify specific abnormalities in people with RTT or in animal models of RTT; studies of transcriptional and post-transcriptional regulation of MECP2 expression in neurodevelopment and neuronal maturation; locus-by-locus and genome-wide analyses of epigenetic dysregulation in animal models of RTT including analyses of associated phenotypic changes; identification of genomic targets of MECP2 actions; development of efficient, sensitive, genome-wide strategies and/or massively parallel methodologies; investigation of the role of MECP2 in other neurological or neurobehavioral disorders, and studies of other conditions and clinical abnormalities that co-occur in the families of individuals with RTT; identification of the downstream molecular targets of MECP2 with a focus on potential molecular targets for drug therapy of RTT; and preclinical screening of potential therapeutic agents including both small-molecule and gene-based therapies in cellular or animal models of RTT.

For more information, potential applicants should contact Dr. Laura Mamounas, Program Director, Neurogenetics Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2132, Bethesda, MD 20892; telephone: 301-496-5745; fax: 301-402-1501; e-mail: lm92t@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAS-06-273.html> (R03), or <http://grants.nih.gov/grants/guide/pa-files/PAS-06-274.html> (R21).

CNS Therapy Development for Lysosomal Storage Disorders Sought

The National Institute of Neurological Disorders and Stroke (NINDS) and the Office of Rare Disorders (ORD) invite grant applications for central nervous system (CNS) therapy development for lysosomal storage disorders.*

Lysosomal storage disorders include about 50 metabolic diseases that collectively affect approximately 1 in 5000 live births. Each of these diseases has heterogeneous pathophysiology and clinical manifestations resulting from deficient activity of specific hydrolases. In some cases, the genetic defect can be in an activator protein for a lysosomal hydrolase or a transporter protein for the metabolites. All of these deficiencies lead to a characteristic pathological accumulation and storage of the substrate for that enzyme in the lysosomes. The consequent accumulation of undigested metabolites in lysosomes leads to multi-systemic dysfunction, including progressive neurologic deterioration, mental retardation, organomegaly, blindness, and early death.

Examples of research topics include, but are not limited to: novel delivery methods for drugs, cells, enzymes, and genes across around the blood-brain barrier (BBB); new types of therapy, including substrate reduction therapy; RNAi-mediated therapy of downstream targets; identification of therapeutic windows of opportunity by characterizing pathophysiological processes; use of non-invasive measures of organ function to identify, characterize, and validate diagnostic biomarkers, intermediate surrogate endpoints, and prognostic biomarkers; estimation of the magnitude of treatment effects based on validated biomarkers that reflect underlying pathogenesis; and development and validation of clinical tools, such as a rating scale or predictor of clinical outcome.

For more information, potential applicants should contact Dr. Danilo Tagle, Program Director, Neurogenetics Group, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2133, Bethesda, MD 20892; telephone: 301-496-5745; fax: 301-402-1501; e-mail: dt39y@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAS-06-202.html>.

Applications Sought for Gene Discovery for Complex Neurological and Neurobehavioral Disorders

The National Institute of Neurological Disorders and Stroke (NINDS) invites applications for research to discover genes for complex neurological and neurobehavioral disorders. This announcement is made together with 3 other components of the National Institutes of Health (NIH).*

Genetic factors contribute to a broad spectrum of neurological and neurobehavioral diseases. During the last decade, genes that cause many single-gene neurological disorders (e.g., Huntington's disease, neurofibromatosis, and Rett syndrome) have been identified. For these disorders, familial inheritance patterns follow the rules of Mendelian segregation. For many common disorders—such as stroke, Parkinson's disease, epilepsy, Alzheimer's disease, and attention deficit hyperactivity disorder—inheritance patterns are more complex, and progress in identifying genes that affect susceptibility and disease outcome has been slow. Such disorders appear to be caused by multiple genes or by a combination of genetic and environmental factors.

Applications responding to this announcement should focus on the identification of susceptibility genes that contribute to genetically complex disorders affecting the nervous system or to the phenotypes that underlie these disorders. Proposed studies can involve the initial collection of biomaterials and clinical information from a patient population or the subsequent application of genetic or molecular strategies for gene localization. Possible methodologies include, but are not limited to, traditional linkage analysis, sib-pair and affected-pedigree-member methods, case-control or family-based association studies, linkage disequilibrium mapping in genetically isolated populations, candidate gene analysis, cytogenetic studies to identify chromosomal abnormalities associated with a disorder, and positional cloning.

For more information, potential applicants should contact Dr. Robert Finkelstein, Director, Division of Extramural Research, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 3307, Bethesda, MD 20892; telephone: 301-496-4370; fax: 301-402-1501; e-mail: rf45c@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAS-06-204.html>.

Research Sought on Genetics and Pathobiology of Vascular Cognitive Impairment

The National Institute of Neurological Disorders and Stroke (NINDS), the National Institute on Aging (NIA), and the National Heart, Lung, and Blood Institute (NHLBI) invite research grant applications aimed at understanding the genetics and pathobiology of vascular cognitive impairment.*

The number of people affected by dementia in the U.S. is expected to increase three-fold in the next 50 years to a total of over 13 million. The best-known form of dementia is Alzheimer's disease (AD), however, a large proportion of dementia cases in the elderly population are not due to AD, but rather to cerebrovascular disease. Dementia due to cerebrovascular disease is referred to as "vascular dementia," and can occur in the absence of AD pathology. In recent years, the term "vascular dementia" has been replaced by the term "vascular cognitive impairment (VCI)."

Research areas of interest include, but are not limited to: genetics of VCI, in both animal models and humans, in particular, identification of genes that render individuals susceptible to cognitive impairment secondary to cerebrovascular disease; analysis of cellular and molecular changes occurring in vascular, neuronal, and glial cells during the development of VCI in humans, and correlation of these with MRI (magnetic resonance imaging) signs and changes in cognitive function; studies of the cellular and molecular bases of the interaction between the VCI and AD pathways; development and characterization of new animal models for the study of VCI, and of the interaction between VCI and AD pathogenic mechanisms; analysis of cognitive function in VCI animal models, and correlation of changes in cognitive function with cellular and molecular pathologies; and studies on the cellular and molecular effects of hypertension, diabetes, hyperlipidemia, coagulant and anticoagulant proteins, inflammatory cytokines, and complement proteins on the vessel wall in appropriate animal models for VCI.

For more information, potential applicants should contact Dr. Gabrielle Leblanc, Program Director, Neurogenetics Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2136, Bethesda, MD 20892; telephone: 301-496-5745; fax: 301-402-1501; e-mail: gl54h@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAS-06-265.html>.

Assays for High-Throughput Screening Sought

The National Institutes of Health (NIH) solicits assays for high-throughput screening (HTS) in the molecular libraries screening centers network (MLSCN).

This program announcement is an NIH Roadmap Initiative. The NIH Roadmap is an innovative approach to accelerate fundamental discovery and translate that knowledge into effective prevention strategies and new treatments. All NIH institutes and centers participate in Roadmap Initiatives.*

The NIH is committed to a major effort to broaden access to HTS technologies and the information produced by these approaches for researchers in academia, government, and non-profit institutions. The objective of this initiative is to invite HTS assay applications to support the MLSCN. The goal of the network is to optimize and implement a variety of innovative biological, biophysical, and cell-based assays for biological targets or processes for which there are limited selective and potent small molecule modulators available to the public.

The MLSCN will provide the following services for assays selected for implementation in this program: assay implementation, compound library, HTS screening, optimization chemistry, and HTS informatics. Assay applications will be evaluated based on: readiness for or adaptability to HTS; assay performance and robustness; and diversity of assay types.

For more information, potential applicants should contact Dr. Ingrid Li, Molecular Libraries Assay Access Project Team, NIH Molecular Libraries and Imaging Roadmap, NIMH, 6001 Executive Boulevard, Room 7185, Bethesda, MD 20892; telephone: 301-443-5288; fax: 301-402-4740; e-mail: ili1@mial.nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at:

<http://grants.nih.gov/grants/guide/pa-files/PAR-06-259.html>.

For more information on the NIH Roadmap, please visit the web site at:

<http://nihroadmap.nih.gov/>.

Research Sought on the Characterization, Behavior, and Plasticity of Pluripotent Stem Cells

The National Institute of Neurological Disorders and Stroke (NINDS) encourages applications for research on the characterization, behavior, and plasticity of pluripotent stem cells. This announcement is made together with 6 other components of the National Institutes of Health (NIH).*

Stem cell research offers enormous potential for treating a host of congenital, developmental, psychiatric, and degenerative diseases for which there are no cures. Stem cells appear to possess great plasticity, but the cellular mechanisms regulating their behavior and fate are not understood. If these mechanisms can be harnessed to obtain cells specifically required for therapy, diagnosis, or drug discovery, it may be possible to restore function to tissues and organ systems that have been compromised by congenital disorders, developmental malfunction, age, injury, disease, or drug exposure.

Areas of research interest include, but are not limited to: comparison of the mitotic potential and fates of different types of pluripotent, progenitor cells in vitro and in vivo; investigation of the ability of different types of stem cells or of partially differentiated cells to revert to a more plastic, multipotent state, under normal conditions and following injury, disease, or drug exposure; examination of changes in gene and protein expression as human and animal stem cells differentiate along specific lineages; development of methods for identifying, isolating, and enriching select precursor populations, intermediate states, and differentiated neuronal and glial phenotypes; use of animal model systems of neurological and neuropsychiatric disorders and of drug addiction for screening and comparing the functional capabilities of implanted stem cells and their progeny; assessment of the ability of transplanted cells to integrate with the adult and aging host nervous system and modify dysfunctional states; and assessment of the effects of environmental changes, therapies, or rehabilitation strategies on the production, differentiation, and survival of endogenous stem cells across the lifespan.

For more information, potential applicants should contact Dr. David Owens, Program Director, Repair and Plasticity Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2204, Bethesda, MD 20892; telephone: 301-496-1447; fax: 301-480-1080; e-mail: do47h@nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PA-06-198.html>.

Collaborative Research in Stem Cell Biology Sought

The National Institute of Neurological Disorders and Stroke (NINDS) invites grant applications for collaborative research in stem cell biology.*

Among the most important biomedical questions are how complex tissues and organs, such as the nervous system, develop from small founder populations of stem cells, how organs are maintained and sometimes regenerate during adult life, and how age and disease affect this capacity. Central to answering all these questions is a profound understanding of the biology and behavior of stem cells. No single investigator, laboratory, or institution has the resources to tackle these complex questions. The solution lies in developing synergy between the various scientific disciplines and investigators with very different expertise and resources.

Areas of research where synergy between different disciplines is of high interest include, but are not limited to: harnessing immune mechanisms to develop tolerance and overcome rejection for use of allogenic cells in the nervous system; defining the transcriptome and proteome of different stem cells and their microenvironment or niche within the host brain and spinal cord; defining co-regulated elements, so-called “hub genes,” in stem cell differentiation toward neuronal or glial phenotypes; evaluating chemical libraries to identify small molecules for stem cell proliferation or neural differentiation; developing cell-based tools for drug discovery, or sensors for the detection and identification of chemical and biological agents that are important for clinical diagnostics for neurological disorders; developing non-invasive methods and agents with which to visualize or track stem cells in vivo; exploring the relationship between stem cells and brain tumors, and identifying factors influencing tumor risk in stem cell therapies; and investigating the use of stem cells as vehicles to deliver targeted therapeutics to sites in the nervous system.

For more information, potential applicants should contact Dr. David Owens, Program Director, Repair and Plasticity Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2204, Bethesda, MD 20892; telephone: 301-496-1447; fax: 301-480-1080; e-mail: do47h@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAS-06-264.html>.

Research Sought on Interactions Between Stem and Progenitor Cells and the Microenvironment

The National Institute of Neurological Disorders and Stroke (NINDS) encourages grant applications for research on the interactions between stem and progenitor cells and the microenvironment. This announcement is made together with 7 other components of the National Institutes of Health (NIH) and is supported by 2 grant funding mechanisms: R21 and R03.*

Stem cell research offers enormous potential for treating many diseases of the nervous system for which there are no treatments or cures. Effective use of stem and progenitor cells for therapeutic purposes hinges on their ability to thrive, integrate, and function in a biologically meaningful manner in vivo without causing adverse events. The objective of this initiative is to promote a thorough exploration and characterization of the bi-directional communication between multipotent cells and the three-dimensional local milieu or niche that they encounter in vivo under normal and compromised states, such as with aging or following injury, disease, or drug exposure.

Areas of research interest include, but are not limited to, studies to: identify, localize, and compare known or novel cues within the developing, adult, and aging nervous system that influence the mitotic potential, cell cycle, and differentiation of stem and progenitor cells along specific lineages; investigate the causal relationship between site-specific changes of endogenous cues resulting from injury, disease, age, exposure to alcohol, drugs of treatment or abuse, and any resulting alterations of stem cell activity; evaluate the effects of external factors such as stress, exercise, or enriched versus impoverished living conditions on the microenvironment within the host organism, and how these changes in microenvironment influence the behavior of stem cells at different periods throughout the lifespan of the organism; and investigate local cellular interactions that determine and maintain the structural and functional integration of progenitor cells into the host nervous system and existing circuitry.

For more information, potential applicants should contact Dr. David Owens, Program Director, Repair and Plasticity Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2204, Bethesda, MD 20892; telephone: 301-496-1447; fax: 301-480-1080; e-mail: do47h@nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at:

<http://grants.nih.gov/grants/guide/pa-files/PAS-06-208.html> (R21), or
<http://grants.nih.gov/grants/guide/pa-files/PAS-06-207.html> (R03).

Research Sought on the Biology of Manual Therapies

The National Institute of Neurological Disorders and Stroke (NINDS) invites grant applications for research on the biology of manual therapies. This announcement is made together with 6 other components of the National Institutes of Health (NIH) and the Canadian Institutes of Health Research (CIHR).*

Manual therapies include a host of techniques that focus primarily on the structures and systems of the body, including bones and joints, soft tissues, and the circulatory and lymphatic systems. Because all body parts are interrelated, common to these approaches to healing is the belief that reducing stresses and improving alignment of the skeleton and its associated soft tissues will elicit the body's innate ability to heal.

Areas of research interest include, but are not limited to: measurement of physiological changes that may result from manual therapies, with emphasis on the nervous system, immune system, endocrine system, and interactions thereof; biomechanical characterization of manual therapies; characterization of normal and pathologic joint and muscle biomechanics, and the impact of manual therapies on the biomechanics of these tissues; development of animal and in vitro models that can be used to study the mechanisms underlying manual therapies; and development of new technologies to study the biomechanics of manual therapies in real time.

For more information, potential applicants should contact Dr. Daofen Chen, Program Director, Systems and Cognitive Neuroscience Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2131, Bethesda, MD 20892; telephone: 301-496-1917; fax: 301-402-1501; e-mail: dc342b@nih.gov.

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*For a full list of supporting components and a more detailed description of this announcement, please visit the NIH web site at:
<http://grants.nih.gov/grants/guide/pa-files/PAR-06-312.html>.

Research Sought on Diet Composition and Energy Balance

The National Institute of Neurological Disorders and Stroke (NINDS) invites grant applications for research on diet composition and energy balance. This announcement is made together with 8 other components of the National Institutes of Health (NIH) and is supported by 2 grant funding mechanisms: R21 and R01.*

Overweight and obesity have increased dramatically in prevalence in the United States. More than 60 percent of the U.S. population is overweight. Environmental changes over the past two decades have increased sedentary behaviors, decreased physical activity, and increased consumption of more energy-dense foods and larger portion sizes. Although an imbalance in energy-consumption and expenditure is required to promote inappropriate weight gain, the relative contributions of each to the burgeoning obesity epidemic remain in dispute.

Topics of research interest include, but are not limited to: the impact of diets varying in levels of protein, carbohydrate, fat, phytochemicals, or ethanol on appetite, food selection and intake, and energy expenditure; the impact of diet composition on neuroendocrine, gastrointestinal, and other factors that may impact energy balance; brain imaging studies in humans and non-human primates to assess positron emission tomography, functional magnetic resonance, or cerebral blood flow imaging responses to specific dietary constituents; development of methods to assess dietary composition; dietary composition effects on the magnitude and time course of neurobehavioral and physiological responses to sleep loss, and the interaction of these effects with BMI, gender, age, and ethnicity; and life-stage, racial/ethnic, and gender-related factors underlying response to diet composition, including studies in children, adolescents, and adults of various ages.

For more information, potential applicants should contact Dr. Merrill Mitler, Program Director, Systems and Cognitive Neuroscience Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2116, Bethesda, MD 20892; telephone: 301-496-9964; fax: 301-402-2060; e-mail: mm777k@nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at:

<http://grants.nih.gov/grants/guide/pa-files/PA-06-174.html> (R21), or
<http://grants.nih.gov/grants/guide/pa-files/PA-06-173.html> (R01).

Research Sought on the Neurobiology of Persistent Pain

The National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute of Dental and Craniofacial Research (NIDCR) invite applications for research on the neurobiology of persistent pain mediated by the trigeminal nerve.*

A diverse group of disorders arises from trauma, pathology, structural or degenerative changes, and sometimes unknown causes that affect the deep tissues of the head and face and often lead to severe, chronic pain. Chronic pain is a debilitating condition that adversely affects the lives of millions of people. Pain disorders mediated by the trigeminal nerve are often associated with severe and persistent pain of deep tissues, which may be of neuronal, muscular, joint, or vascular origin.

Potential areas of research interest include, but are not limited to: development of model systems that appropriately mimic the clinical features of syndromes associated with deep tissue pain in the head and neck region to provide optimal tools for basic and clinical studies; discovery of mechanisms of plasticity at the neurochemical, molecular, and cellular levels, which contribute to abnormal pain responses (hyperalgesia, allodynia) and persistent pain associated with disorders of tissues innervated by the trigeminal nerve; neuroimaging of pain-signaling pathways to elucidate the roles of central and peripheral plasticity in mediating the onset, persistence, and management of chronic pain associated with migraine and other pain disorders of the head and neck; elucidation of the role of acid-sensitive ion channels in deep tissues of the head and neck in onset of pain and the development of abnormal pain responses and chronic pain; characterization of sensory, cognitive, affective, and other biobehavioral responses to noxious stimulation and pain perception in humans; determination of the usefulness of exercise in pain management through clinical trials; and development and testing of novel mechanism-based therapies for improved management of chronic pain associated with craniofacial disorders through appropriate clinical trials.

For more information, potential applicants should contact Dr. Linda Porter, Program Director, Systems and Cognitive Neuroscience Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2113, Bethesda, MD 20892; telephone: 301-496-9964; fax: 301-402-2060; e-mail: lp216a@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAS-06-199.html>.

Research Sought on Methodology and Measurement in the Behavioral and Social Sciences

The National Institute of Neurological Disorders and Stroke (NINDS) encourages grant applications for research on methodology and measurement in the behavioral and social sciences. This announcement is made together with 12 other components of the National Institutes of Health (NIH) and is supported by 2 grant funding mechanisms: R21 and R03.*

Methodology and measurement encompass research design, data collection, measurement, and data analysis. The goal of this announcement is to encourage research that will improve the quality and scientific power of data collected in the behavioral and social sciences, relevant to the missions of NIH.

Research areas of interest include, but are not limited to, methodology and measurement issues: in developing innovative interdisciplinary, multi-method, and multilevel research designs for use in behavioral and social science research, with special emphasis on both developing new technologies and addressing the analytical complexities associated with the integration of behavioral, social, and biological data; in research relating to diverse populations, for example, populations that are distinctive by virtue of age, gender, sexual orientation, ethnicity, culture, including culture-specific medical systems, socio-economic status, literacy, language, or disability; in studying how dramatic changes in economic, social, environmental, physical, or political context affect human health and well-being, including developing new methods if older ones are no longer valid in the face of significant changes in populations and societies over the last several decades; in studying potentially sensitive behaviors, such as sexual behavior and abortion, and covert or illegal behaviors such as drug use, abuse, and violence; and concerning ethics in research, with emphasis on the topics of informed consent, assessment of risk and benefit, selection and retention of subjects, and ensuring subjects' confidentiality.

For more information, potential applicants should contact Dr. Deborah Olster, Office of Behavioral and Social Sciences Research, NIH, Building 31, Room B3237, 31 Center Drive, Bethesda, MD 20892; telephone: 301-402-1147; e-mail: olsterd@od.nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at:

<http://grants.nih.gov/grants/guide/pa-files/PA-06-343.html>, or
<http://grants.nih.gov/grants/guide/pa-files/PA-06-344.html>.

Neurotechnology Research, Development, and Enhancement Sought

The National Institute of Neurological Disorders and Stroke (NINDS) invites applications for neurotechnology research, development, and enhancement. This announcement is made together with 7 other components of the National Institutes of Health (NIH) and is supported by 2 grant funding mechanisms: R21 and R01.*

In biomedicine, new tools and approaches often make possible tremendous advances in research on health and disease, and sometimes shift the manner in which such research is undertaken and results are interpreted. The brain, and its product and behavior, represent a spectacularly complex system. Despite this, brain and behavioral sciences are rapidly advancing, with important discoveries coming to light daily. These discoveries will improve understanding of healthy brain function and offer promise to the millions suffering from brain disorders of all types. To accelerate the pace of discovery, new tools and approaches are needed.

Examples of hardware, software, and wetware appropriate for this announcement include, but are not limited to: informatics tools for analyzing, organizing, querying, integrating, sharing, or visualizing data about the brain or behavior; genetic approaches to study structure or function of neural circuits in animal models; non-invasive methods for in vivo tracking of implanted cells; tools for real-time analysis of neurophysiological events; probes of brain gene expression that can be imaged non-invasively; tools, technologies, and algorithms for neuroprosthesis development; tools to enhance visualization of specific brain markers; new methods or agents to study neural connectivity in living or postmortem brain; devices for non-invasive diagnosis and precise identification of pathogens involved in central and peripheral neural infectious diseases; non-invasive optical imaging approaches; technologies for detection, intervention, and prevention of acute, adverse neurological events; biomarkers to indicate existence of, or change in, brain disorders; and technologies to facilitate high-throughput analysis of behavior.

For more information, potential applicants should contact Dr. Daofen Chen, Program Director, Systems and Cognitive Neuroscience Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2131, Bethesda, MD 20892; telephone: 301-496-1917; fax: 301-402-1501; e-mail: dc342b@nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at:

<http://grants.nih.gov/grants/guide/pa-files/PA-06-278.html> (R21), or
<http://grants.nih.gov/grants/guide/pa-files/PA-06-279.html> (R01).

Sleep and Sleep Disorders Research Sought

The National Institute of Neurological Disorders and Stroke (NINDS) invites grant applications for research on sleep and sleep disorders. This announcement is made together with 12 other components of the National Institutes of Health (NIH).*

An estimated 70 million people in the United States suffer from sleep problems, and more than 50 percent of them have a chronic sleep disorder. Each year, sleep disorders, sleep deprivation, and excessive daytime sleepiness add approximately \$16 billion to the cost of health care in the U.S. and result in \$50 billion in lost productivity. Despite substantial scientific progress in both clinical and basic science related to sleep and its disorders, there remains the challenge and the need to better understand the functions of sleep, to better understand and treat disorders affecting sleep, and to explain the nature of human physiology during wakefulness and the individual stages of sleep.

Topics of research interest include, but are not limited to: neurobiology and functions of sleep and neurochemistry of sleep/wake generating systems from fetal life across the full age spectrum, including molecular, biochemical, anatomic, and physiologic investigations; exploration of the physiologic basis for the restorative function of sleep in maintenance of health; methods to measure sleep, circadian physiology, and sleepiness across the age spectrum, including methods used in the home; interventions to help children and adults adapt to the sleep disturbance associated with homes, hospitals, critical care settings, and nursing homes; studies of normal human sleep phenotypes and the normal range of variation in children, adults, and the aged (including racial and ethnic disparities), and quantitative assessment of sleep variables such as duration, sleep stage distribution and sleep quality; and studies of sleep problems and disorders in children related to chronic maternal use of alcohol, cigarette smoking, and narcotic drugs.

For more information, potential applicants should contact Dr. Merrill Mitler, Program Director, Systems and Cognitive Neuroscience Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2116, Bethesda, MD 20892; telephone: 301-496-9964; fax: 301-402-2060; e-mail: mm777k@nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PA-06-238.html>.

Research Sought on Temporomandibular Joint and Muscle Disorders

The National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Dental and Craniofacial Research (NIDCR), and the Office of Research on Women's Health (ORWH) invite grant applications for research on the etiological and pathophysiological mechanisms underlying a set of chronic, comorbid conditions associated with temporomandibular joint and muscle disorders (TMJMDs). This announcement is supported by 3 grant funding mechanisms: R03, R21, and R01.*

TMJMD, a complex heterogeneous disease, represents a collection of disorders with varying causes, affecting the tissues of the masticatory muscles and the temporomandibular joint. Due to this complexity and a lack of complete understanding of the underlying mechanisms of disease onset and progression, treatment for TMJMD currently is less than satisfactory.

Examples of research topics may include, but are not limited to: identification of molecular mechanisms in the central nervous system that modulate peripheral nociceptive neurotransmission; genomic studies that identify genes and gene polymorphisms that are causative or produce risk factors for comorbid conditions and TMJMD; effects of inflammatory pain and proinflammatory cytokines on hypersensitivity of central pain modulatory circuits; neuroimaging studies to identify brain regions and nerve tracts active in patients with TMJMD and comorbid conditions; use of animal models to examine the effects of chronic pain on affective behaviors; and clinical research approaches that help to discover behavioral changes influencing and influenced by TMJD and comorbid conditions.

For more information, potential applicants should contact Dr. Linda Porter, Program Director, Systems and Cognitive Neuroscience Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2113, Bethesda, MD 20892; telephone: 301-496-9964; fax: 301-402-2060; e-mail: lp216a@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PA-06-267.html> (R03), <http://grants.nih.gov/grants/guide/pa-files/PA-06-268.html> (R21), or <http://grants.nih.gov/grants/guide/pa-files/PA-06-188.html> (R01).

Exploratory/Developmental Projects in Translational Research Sought

The National Institute of Neurological Disorders and Stroke (NINDS) encourages applications for exploratory or developmental projects in translational research.*

Translational research applies ideas, insights, and discoveries generated through basic scientific inquiry to the treatment or prevention of human disease. In many cases, developmental work must be completed before the basic research results can be translated into effective therapies. A key requirement for successful therapeutic development is the characterization of new assays, models, tools, and technologies that provide for reliable discovery and testing of therapeutic approaches.

Areas of research interest include, but are not limited to: identification of targets for therapeutic intervention; development of assays that permit preliminary screening of candidate therapeutics; animal model development for further evaluation of candidate therapeutics and/or toxicology studies; development of tools and technologies that can be directly used for therapy development; preliminary identification of candidate therapeutics that can be evaluated through further preclinical testing; and testing of therapeutics for efficacy in cell-based or animal models of a neurological disorder.

For more information, potential applicants should contact Dr. Thomas Miller, Program Director, Technology Development Group, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2139, Bethesda, MD 20892; telephone: 301-496-1779; fax: 301-402-1501; e-mail: tm208y@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAR-06-189.html>.

Exploratory Collaborations with National Centers for Biomedical Computing Sought

The National Institute of Neurological Disorders and Stroke (NINDS) encourages applications for exploratory collaborations with national Centers for Biomedical Computing (NCBCs). This announcement is made together with 12 other components of the National Institutes of Health (NIH).*

The NIH NCBCs are the hubs of a networked national effort to build the computational infrastructure for biomedical computing in the nation. The centers are devoted to all facets of biomedical computing—from basic research in computational science to providing the tools and resources that biomedical and behavioral researchers need to do their work. In addition to carrying out fundamental research, the centers play a major role in educating and training researchers to engage in biomedical computing, and provide tools and resources that biomedical and behavioral researchers can use at a variety of levels.

Areas of research interest include, but are not limited to: behavioral science; biological rhythms; biomedical imaging; cell biology; demographic and social science; developmental biology; drug design at the molecular and cellular levels; dynamic modeling of health, chronic disease, and disablement; environmental health science; epidemiology; genetics; genomics; immunology/inflammation; infectious disease; informatics support for diagnosis and clinical decision-making; medical genetics; morphology; neurobiology and cognitive science; pharmacology and toxicology; physiology; population biology; structural biology; substance abuse research; surgery and virtual tools; and systems biology and signal transduction pathways and networks.

For more information, potential applicants should contact Dr. Yuan Liu, Chief, Office of International Activities, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2187, Bethesda, MD 20892; telephone: 301-496-1917; fax: 301-402-1501; e-mail: yl5o@nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/pa-files/PAR-06-223.html>.

International Neuroscience Fellowship Applications Sought

The National Institute of Neurological Disorders and Stroke (NINDS) invites applications for international neuroscience fellowships. This announcement is made together with 3 other components of the National Institutes of Health (NIH).*

The goals of the international neuroscience fellowship program are to advance the training of qualified foreign neuroscientists by enhancing their basic or clinical research skills in a research setting in the United States and to prepare awardees for future leadership positions in research, academia, or public health institutions in their home country. The program will strengthen the human resource capital of neuroscience research in foreign institutions, particularly those with limited economic resources, and enhance the quality and quantity of international neuroscience research, while fostering long-lasting collaborations between foreign and U.S. neuroscientists.

Fellowships supported under this announcement are expected to have high relevance to the mission of NINDS, particularly as it relates to brain and nervous system disorders in low- to middle-income countries. NINDS aims to support collaborative training programs between U.S. neuroscience researchers and foreign investigators that focus on studies in the areas of ion channels, synapses and circuits, neural signaling and pathways, neural genetics and neural development, motor control, motor-sensory integration, brain repair and plasticity, cognition and behavior, and neurodegenerative and other neurological disorders. Specific disease areas of interest include, but are not limited to, stroke, epilepsy, Parkinson's disease, multiple sclerosis, neurological consequences of AIDS, muscular dystrophy, and autism. NINDS encourages basic, translational and clinical research on the normal and diseased nervous system, clinical trials of interventions of therapeutic modalities, and epidemiological research to identify risk factors and to establish prevalence and incidence estimates of pathologic conditions.

For more information, potential applicants should contact Dr. Yuan Liu, Chief, Office of International Activities, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2187, Bethesda, MD 20892; telephone: 301-496-1917; fax: 301-402-1501; e-mail: yl5o@nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at:
<http://grants.nih.gov/grants/guide/pa-files/PAR-06-227.html>.

Applications Sought for Ruth L. Kirschstein National Research Service Awards for Individual Postdoctoral Fellows

The National Institute of Neurological Disorders and Stroke (NINDS) encourages applications for Ruth L. Kirschstein National Research Service Awards (NRSA) for Individual Postdoctoral Fellows. This announcement is made together with 20 other components of the National Institutes of Health (NIH).*

The objective of the NRSA is to provide support to promising postdoctoral applicants who have the potential to become productive and successful independent research investigators in scientific health-related fields relevant to the missions of the participating NIH institutes and centers.

The proposed postdoctoral training must be within the broad scope of biomedical, behavioral, or clinical research or other specific disciplines relevant to the NIH research mission, and must offer an opportunity to enhance the fellow's understanding of the health-related sciences and extend his or her potential for a productive research career.

For more information, potential applicants should contact Dr. Stephen Korn, Director, Training and Career Development, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2186, Bethesda, MD 20892; telephone: 301-496-4188; fax: 301-594-5929; e-mail: NINDStrainingoffice@ninds.nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at:
<http://grants.nih.gov/grants/guide/pa-files/PA-06-373.html>.

NIH Exploratory/Development Research Grant Program Applications Sought

The National Institute of Neurological Disorders and Stroke (NINDS) invites applications for the National Institutes of Health (NIH) exploratory/development research grant program. This announcement is made together with 16 other components of the NIH.*

The evolution and vitality of the biomedical sciences require a constant infusion of new ideas, techniques, and points of view. These may differ substantially from current thinking or practice and may not yet be supported by substantial preliminary data. The NIH seeks to foster the introduction of novel scientific ideas, model systems, tools, agents, targets, and technologies that have the potential to substantially advance biomedical research. This initiative is intended to encourage new exploratory and developmental research projects that may involve considerable risk but lead to a breakthrough in a particular area, or to the development of novel techniques, agents, methodologies, models, or applications that could have a major impact on a field of biomedical, behavioral, or clinical research.

Applications submitted under this initiative should be exploratory and novel. The studies should break new ground or extend previous discoveries toward new directions or applications. Long-term projects and projects designed to increase knowledge in a well-established area will not be considered.

For more information, potential applicants should contact the NINDS Referral Officer; telephone: 301-496-9223; e-mail: nindsreview.nih.gov@mail.nih.gov.

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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at:
<http://grants.nih.gov/grants/guide/pa-files/PA-06-181.html>.

NIH Small Research Grant Program Applications Sought

The National Institute of Neurological Disorders and Stroke (NINDS) invites applications for the National Institutes of Health (NIH) small research grant program. This announcement is made together with 12 other components of the NIH.*

The NIH small research grant program supports small investigator-initiated research projects that can be carried out in a short period of time with limited resources. Investigator-initiated research, also known as unsolicited research, is funded as a result of an investigator submitting a research grant application to NIH in his or her area of interest and competency.

This grant mechanism supports different types of projects including pilot and feasibility studies; secondary analysis of existing data; small, self-contained research projects; development of research methodology; and development of new research technology.

For more information, potential applicants should contact the NINDS Referral Officer; telephone: 301-496-9223; e-mail: nindsreview.nih.gov@mail.nih.gov.
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*For a full list of supporting NIH components and a more detailed description of this announcement, please visit the NIH web site at:
<http://grants.nih.gov/grants/guide/pa-files/PA-06-180.html>.

Applications Requested for Network for Cardiothoracic Surgical Investigations in Cardiovascular Medicine

The National Institute of Neurological Disorders and Stroke (NINDS), the National Heart, Lung, and Blood Institute (NHLBI), and the Institute of Circulatory and Respiratory Health (CRH) of the Canadian Institutes of Health Research (CIHR) invite applications to participate in the Network for Cardiothoracic Surgical Investigations in Cardiovascular Medicine—a cooperative network of academic centers with clinically active cardiothoracic surgeons and their colleagues in allied specialties interested in promulgating the use of evidence-based medicine in surgical practice. *

The goal of the network is to foster a culture of rigorous scientific comparisons and promote the evaluation of newer surgical techniques, technologies, devices, and innovative pharmaceutical and bioengineered products directed at cardiovascular disease. The network will allow research teams to evaluate newer therapies and techniques as they move from laboratory science to broad clinical use, and will enhance the capacity to disseminate study results, and translate findings to large-scale trials or practice. The program will provide support to maintain the necessary infrastructure to develop, coordinate, and conduct multiple collaborative proof-of-concept clinical studies and interventional protocols to improve cardiovascular disease outcomes.

Research topics include, but are not limited to: neuroprotective techniques, agents and devices to prevent central nervous system complications of cardiac surgery; studies comparing minimally invasive surgery to catheter-based ablation approaches for the treatment of chronic atrial fibrillation; clinical testing of new heart valve repair techniques; clinical testing in adults with congenital heart disease of surgery to treat atrial and ventricular arrhythmias; trials of new computer-enhanced modalities for imaging, instrumentation, and robotics for minimally invasive cardiac surgery; and clinical studies of peri-operative techniques and/or drugs to reduce injury from spinal cord ischemia in patients undergoing repair of thoracic and thoraco-abdominal aortic conditions, including aortic dissections and aneurysms.

Letters of Intent Receipt Date: July 28, 2006

Application Receipt Date: August 28, 2006

For more information, potential applicants should contact Dr. Claudia Moy, Clinical Research Project Manager, Clinical Trials Group, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2214, Bethesda, MD 20892; telephone: 301-496-2789; fax: 301-480-1080; e-mail: cm384s@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-06-005.html>.

Research Requested on Nuclear Structure-Function Defects in the Pathogenesis of Muscular Dystrophy

The National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), and the Muscular Dystrophy Association (MDA) invite applications for research on the nuclear structure-function defects in the pathogenesis of muscular dystrophy. This announcement is supported by 2 grant funding mechanisms: R21 and R01.*

The muscular dystrophies are hereditary, degenerative disorders affecting cardiac and skeletal muscle. Despite substantial research efforts, there are few therapies that are effective at slowing the course of muscular dystrophy.

Areas of research interest include, but are not limited to: basic cellular and molecular studies that link changes in nuclear structure and function to the specific pathologies that are associated with Emery-Dreifuss, facioscapulohumeral, limb girdle muscular dystrophy 1B, and oculopharyngeal muscular dystrophy; studies of disrupted chromatin organization, gene expression, RNA processing, DNA replication and repair, vulnerability to nuclear stress and apoptosis, anchorage of nuclear envelope proteins, and transport mechanisms between the nucleus and cytoplasm in this subset of muscular dystrophies; studies of altered gene transcription as a consequence of impaired mechanotransduction in this subset of muscular dystrophies; studies that determine the underlying mechanisms responsible for the tissue- and muscle group-specificity seen in this subset of muscular dystrophies; studies that address the role of nuclear dysfunction in the impaired myoblast activation, delayed differentiation kinetics, and impaired myogenic terminal differentiation programs seen during myogenesis and the impaired muscle regeneration capacity observed in the nucleus-based muscular dystrophies; and studies that develop appropriate cell- and model organism-based systems and use these to characterize nuclear events in the pathogenesis of this subset of muscular dystrophies.

Letters of Intent Receipt Date: August 21, 2006

Application Receipt Date: September 20, 2006

For more information, potential applicants should contact Dr. John Porter, Program Director, Channels, Synapses, and Circuits Cluster, NINDS, Neuroscience Center, 6001 Executive Boulevard, Room 2142, Bethesda, MD 20892; telephone: 301-496-1917; fax: 301-402-1501; e-mail: jp477n@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-07-002.html> (R21), or <http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-07-001.html> (R01).

Applications Requested for Rehabilitation Research Career Development Programs

The National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute of Child Health and Human Development (NICHD) request applications for rehabilitation research career development programs.*

Despite the increasing population of individuals coping with chronic disabilities at various levels, the field of medical rehabilitation has not responded sufficiently to the need for research to validate approaches, optimize treatments, and incorporate new technologies and opportunities. Unprecedented opportunities exist to explore the biomedical, behavioral, and social bases for rehabilitative strategies and their application to appropriate populations. This announcement invites applications to coordinate the mentoring and career development of rehabilitation researchers in one of 3 domains: allied health professionals, clinicians involved in neurological rehabilitation, or engineers.

The program will be responsible for, but not limited to: developing guidelines for mentoring, didactic interactions, career development, and the responsible conduct of research; developing and promoting a network of established faculty with a record of research support and productivity who could serve as potential mentors and secondary resources for scholar candidates; negotiating and coordinating with participating institutions and departments to ensure that scholars obtain appropriate research support and opportunities for advancement; recruiting, selecting, and supporting those individuals who would most benefit from participation in this program and are most likely to develop independent careers in medical rehabilitation research; periodically reviewing the research and career goals of each individual in conjunction with their mentor; providing special opportunities for research presentations and professional advancement, and assistance in career counseling and job placement; and enhancing the involvement of women, individuals from underrepresented racial and ethnic groups, and persons with disabilities as candidates, mentors, and/or other resource positions.

Letters of Intent Receipt Date: August 22, 2006

Application Receipt Date: September 22, 2006

For more information, potential applicants should contact Dr. Ralph Nitkin, National Center for Medical Rehabilitation Research, NICHD, 6100 Executive Boulevard, Room 2A03, Bethesda, MD 20892; telephone: 301-402-4206; e-mail: rn21e@nih.gov.

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*For a more detailed description of this announcement, please visit the NIH web site at: <http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-06-010.html>.

Patients with Cervical or Focal Hand Dystonia Sought

Scientists at the National Institute of Neurological Disorders and Stroke (NINDS) seek people with cervical or focal hand dystonia who are receiving botulinum toxin injections for a study of a medication called amlodipine. This research study will examine whether amlodipine can improve the effect of botulinum toxin injections for dystonia, which causes abnormal postures and disrupted movements.

The study will be conducted at the National Institutes of Health (NIH) Clinical Center in Bethesda, MD. All study-related expenses will be paid by the NIH.

For more information, physicians should contact Dr. Barbara Karp, Office of the Clinical Director, NINDS, NIH, Building 10, Room 5S209, 10 Center Drive MSC 1428, Bethesda, MD 20892-1428; telephone: 301-496-0150; fax: 301-480-2973. Please refer to study number 01-N-147.

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